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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/719,336	03/22/2001	Mangus Von Knebel-Docberitz	4121-121	7154

7590 01/28/2003

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EXAMINER
QIAN, CELINE X

ART UNIT	PAPER NUMBER
1636	15

DATE MAILED: 01/28/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/719,336	VON KNEBEL-DOEBERITZ ET AL.	
	Examiner	Art Unit	
	Celine X Qian	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11 and 13-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11 and 13-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 1-11 and 13-15 are pending in the application.

This Office Action is in response to the Response filed on 12/13/02. The Amendment filed on 9/3/02 has been entered.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/13/02 has been entered.

Response to Amendment

The rejection of claims 1-6 and 10-12 under 35 U.S.C. 112 second paragraph has been withdrawn in light of Applicants' amendment of the claims.

Claims 1-6, 10-12 and newly added claims 13-15 are rejected under 35 U.S.C. 112 first paragraph for reasons set forth of the record mailed on 1/17/02 and 7/2/02.

Response to Arguments

Claims 1-11 and 13-15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In response to the 112 first paragraph rejection, Applicants argue that ample disclosure regarding the effective amount of the pharmaceutical composition comprising the AAV2 virus

and the route of administration of said composition have been provided in the specification for practicing present invention. Applicants further argue that the specification have presented data in both mouse model and small cell lung cancer lines, thus have gone the extra step recommended by NCI. Applicants alleges that the patents office lack continuity in prosecuting the current application and cite a number of patents regarding cancer treatment. Applicants indicate that these patents only discuss testing methods limited to cancer cell testing and/or nude mouse testing but they are allowed to encompass human subjects. According to these standard, Applicants assert that the teaching and the working examples provided by the instant specification is sufficient to support the enablement of the claimed invention.

These arguments have been considered, however, deemed not persuasive. Applicants misconstrue that the rejection is based only on lack of teaching from the specification in regard to effective amount and route of administration. The rejection made of record established a prima facie case of non-enablement based on both the highly unpredictable nature of the claimed invention and the apparent lack of teachings/guidance from the present specification that is commensurate in scope with the broadly claimed invention.. At the time of filing, the relevant art considered gene therapy as a whole to be unpredictable as modes of delivery that would provide efficient delivery and expression of genes encoding the protein in the target cells had not been developed. Clinical efficacy has not been achieved in any gene therapy protocol to date (see Verma et al., Gene Therapy promises, problems and Prospects, Nature, Vol. 389, p.239, col., 1). In cancer treatment, only intratumoral administration of vectors resulted in some success. Although the specification teaches administering AAV2 at 109-1010 particle/kg body weight intravenously, intratumorally, orally or cutaneously, it does not provide support that these

methods of delivery can overcome the technical difficulties that existed in the art and achieve successful therapy in human subjects. The example provided by the specification only teaches intratumoral injection to deliver AAV2 virus. Therefore, the claimed method is at most enabled for intratumoral delivery of AAV2 virus. Since the claimed method encompass all routes of administration, one skilled in the art would have to engage in undue experimentation to practice the claimed method to its full scope.

Applicants state that the Gura article considers the use of cancer cells as an appropriate and applicable testing method to augment nude mouse testing for cancer treatments. It appears that Applicants misconstrue the teaching of article by selectively choosing only a section of the article. Contrary to Applicants assertion, the Gura article discusses the problems that exist in the current systems for identifying new drugs. Right after the paragraph cited by the Applicants, the article states "Over the last 7 years, the panel has been used to screen almost 63,000 compounds, and 5000 have exhibited tumor cell-killing activity. But that has created another dilemma, because so many compounds show antitumor cell activity in culture, and the cost of bringing them all to clinical trials-where most don't work anyway- would be daunting." Therefore, as discussed in the previous office action, antitumor drugs in xenograft murine models and in vitro cell culture is not predictive of their efficacy in human subjects. As such, one skilled in the art would have to engage in undue experimentation to practice the claimed invention.

Applicants' argument that the examination lacks continuity in considering the current application compare to a number of issued patent is neither persuasive nor on the point because an issued patent is a property, not a precedent. Each patent is examined based on its own merits.

Therefore, the cited patents cannot be relied upon as standards for examination of the present application.

Applicants' declaration has been fully considered, however, is not sufficient to support the enablement of the claimed invention. Applicants disclose the sensitization of a implanted pancreas tumor in an immunocompetent rat model to chemotherapeutic agent 5-FU. Applicants demonstrated that intratumoral AAV2 administration prior to treatment with 5-FU significantly reduced tumor growth compare to 5-FU treatment alone. Applicants further disclose that the chemotherapy-related toxic effects are reduced in the animals with concomitant AAV2 administration. However, Applicants do not disclose whether these tumor cells are resistant to chemotherapy or radiotherapy. This is an important piece of information that is necessary to support the enablement of the claimed method because the invention is drawn to a method for lowering chemotherapy or radiotherapy induced resistance by infecting patients with AAV2. Therefore, the declaration does not support the enablement of the claimed method.

Therefore, the 112 first paragraph rejection is maintained.

Personal interview

Applicants indicate a discussion of the case with Examiner and Supervisory Examiner is requested if the rejection is maintained. Such interview can be set up at Applicants' convenience.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X Qian whose telephone number is 703-306-0283. The examiner can normally be reached on 9:00-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 703-305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Celine Qian, Ph.D.
January 26, 2003

Anne-marie Falk

ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER